

Remarks

Claims 1-20 are pending in the application. Claims 6-12 are withdrawn from consideration. Claim 1 is amended. Support for the amendment to claim 1 can be found, for example, at page 25, lines 7-8 of the instant specification.

Applicants also bring the Examiner's attention to a Petition submitted March 24, 2004 To Correct Inventorship to add Etienne Pages as co-inventor on the above-referenced application.

The Examiner has maintained rejections of the claims for anticipation and obviousness.

Rejection under 35 USC 102(b)

Claims 1 and 2 are rejected as anticipated by Meryman *et al.*, WO91/04659 ("Meryman"). The rejection is traversed.

Claim 1 as amended, from which depends claim 2, requires that (a) the wash solution contain chloride, and (b) that the concentration of DPG in the blood cell suspension falls to greater than or equal to approximately half of its initial concentration at 21 days.

None of the solutions described by Meryman have both of these features. With respect to the ADSOL, ARC8 and a buffered saline solution with 154 mM NaCl (disclosed in Example 2, on pages 27-28 of Meryman) cited by the Examiner, Applicants submit that ADSOL is not a wash solution (emphasis added). Instead, ADSOL is a storage solution, as defined by the instant specification, *i.e.* a solution blood cells are contained in for prolonged periods.¹ Meryman teaches instead that ADSOL is used as a "preservation solution" for red blood cells after, "blood is conventionally drawn into a solution containing *only citrate, phosphate and glucose* at pH

¹ See, *e.g.* the instant specification at page 2, lines 24-25.

5.7.”² (Emphasis added). Meryman teaches that ADSOL is used as a preservation or storage solution after washing the cells with a wash solution that does not contain chloride. Thus, the disclosure of ADSOL in Meryman is not related to the use of ADSOL as a wash solution, and the teachings of Meryman related to ADSOL do not anticipate claims 1 or 2.

ARC8 does not contain chloride.³ Thus, the teachings of Meryman related to ARC8 do not meet the requirement of claim 1 that the wash solution contain chloride.

The buffered saline solution with 154 mM NaCl, disclosed in Example 2, on pages 27-28 of Meryman, does not maintain the DPG concentration of the red blood cells after 21 days at approximately half of the initial DPG concentration or greater, as stipulated in claim 1, as amended. The results of the storage experiments described in Example 2 of Meryman are described in Figure 5. The DPG levels of red blood cells washed in saline and stored for 2 weeks were below 20%, and apparently were too low to be measured after this point. The teachings of Meryman related to a 154 mM NaCl solution therefore do not describe the features of claim 1. Applicants request reconsideration and withdrawal of the rejection for anticipation.

Rejection under 35 USC 103(a)

Claims 1-5 and 13-20 remain rejected as unpatentable over Meryman and Edson *et al.*, WO00/18969 (“Edson”). Applicants traverse this rejection in light of the amendment to claim 1.

As explained above, Meryman does not teach or suggest the use of a wash solution containing saline used in the process of storage of blood wherein DPG falls to greater than or equal to approximately half of its initial concentration at 21 days. Rather, the only use of a saline containing wash solution disclosed in Meryman reduces DPG concentrations well below 50% of

² See Meryman at page 1, lines 25-28.

³ *Id.* at page 17, Table 2.

the initial concentration after 21 days.⁴ DPG levels in stored red blood cells are used as a measure of maintenance of red blood cell metabolism.⁵ Studies on red blood cells have focused on maintaining DPG concentrations in the cells for as long as possible.⁶

Edson does not remedy the deficiencies of Meryman because it does not teach the long term storage of red blood cells at 4 °C after washing with a wash buffer containing chloride. Edson reports that washed cells were only stored for 18 hours (*see* page 25, lines 25-26 and page 31, lines 11-16 of Edson). Other blood cells washed with saline were frozen when stored, not kept at 4°C (*see* page 29, lines 2-5 of Edson). No mention of DPG level was made in Edson.

There is no *prima facie* case of obviousness shown by the combination of Meryman and Edson. To establish a *prima facie* case of obviousness, the prior art references must teach or suggest all the claim limitations.⁷ The combination of Meryman and Edson do not teach washing cells with a wash solution containing saline in which DPG levels are equal to or greater than 50% of their initial levels after 21 days. Further, the invention of claims 1-5 and 13-20 shows the unexpected property of maintaining DPG levels at or above 50% after 21 days of storage despite being washed in a wash solution containing saline, as opposed to the teaching of Meryman. Presence of an unexpected property not shown in the prior art is evidence of nonobviousness.⁸ For the above reasons, Applicants request that this rejection be withdrawn.

Claims 1-5 and 13-20 are further rejected as unpatentable for obviousness over Meryman and Edson in light of Sharma U.S. Patent No. 6,235,239 (“Sharma”). The Examiner asserted, on page 9 of the Office Action, that Sharma teaches a method of washing red blood cells with a

⁴ *Id.* at Figure 5.

⁵ Leonart *et al.* Sao Paulo Med J 118(2):41-5 (2000) at 41. Included, herewith, as Exhibit A.

⁶ *Id.*

⁷ MPEP § 2142.

⁸ MPEP § 716.02(a).

sterile phosphate buffered saline solution and storing the cells for 20 days in a refrigerator.

Applicants traverse this rejection in light of the amendment to claim 1.

The teachings of Sharma do not remedy the deficiencies of Meryman and Edson described above. Sharma does not teach the DPG levels of these red blood cells, nor does it teach any characteristics of the cells from which the DPG levels could be inferred. The purpose of these teachings of Sharma was to compare the red blood cell count, hemoglobin and hematocrit levels of cells that were treated with the anti-viral compound B, to control cells, to see if there was any side effects of the treatment. While Sharma teaches that the exposure of red blood cells with compound B does not seem to have a significant differential effect on red blood cell count, hemoglobin or hematocrit among cells treated or not treated with compound B, all of the cells washed with saline and stored for 20 or 39 days⁹ showed a decrease in red blood cell count, hemoglobin and hematocrit.¹⁰

As explained above, Meryman teaches that washing red blood cells in saline solution causes a drop in DPG below 50% of initial DPG. Thus, the addition of the teachings of Sharma to the teachings of Meryman and Edson, do not teach or suggest all of the limitations of the claims as amended. Further, the properties of the saline wash solutions described in the instant specification are still unexpected in light of the combination of Meryman, Edson and Sharma. Sharma does not teach or suggest the unexpected stability in DPG levels of red blood cells during storage after being washed in a saline solution. Thus, the invention of the instant claims also produces unexpected results in light of the combination of Meryman, Edson and Sharma. Thus, in light of the above arguments, Applicants request that this rejection be withdrawn

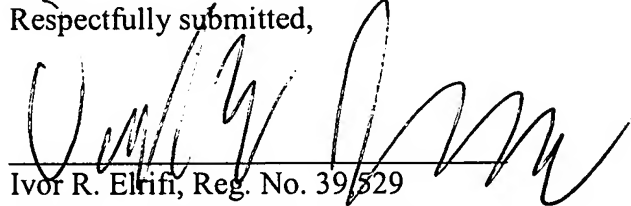
⁹ It is unclear how long the cells were stored for. The text at the bottom of column 20 and the asterisk in Table X say 20 days, but the subtitle of Table XI says 39 days.

¹⁰ *Id.* at column 21, Tables IX and X.

In view of the foregoing comments, Applicants request reconsideration and withdrawal of the rejection for obviousness.

The Commissioner is authorized to charge any fees that may be due to Deposit Account No. 50-0311, (Reference No. 18242-508 CIP2).

Respectfully submitted,



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